Does Telomere Length Explain Race/Ethnic Differences in Aging among Older Adults?: Evidence from the Health and Retirement Study

LAUREN BROWN, PHD, MPH

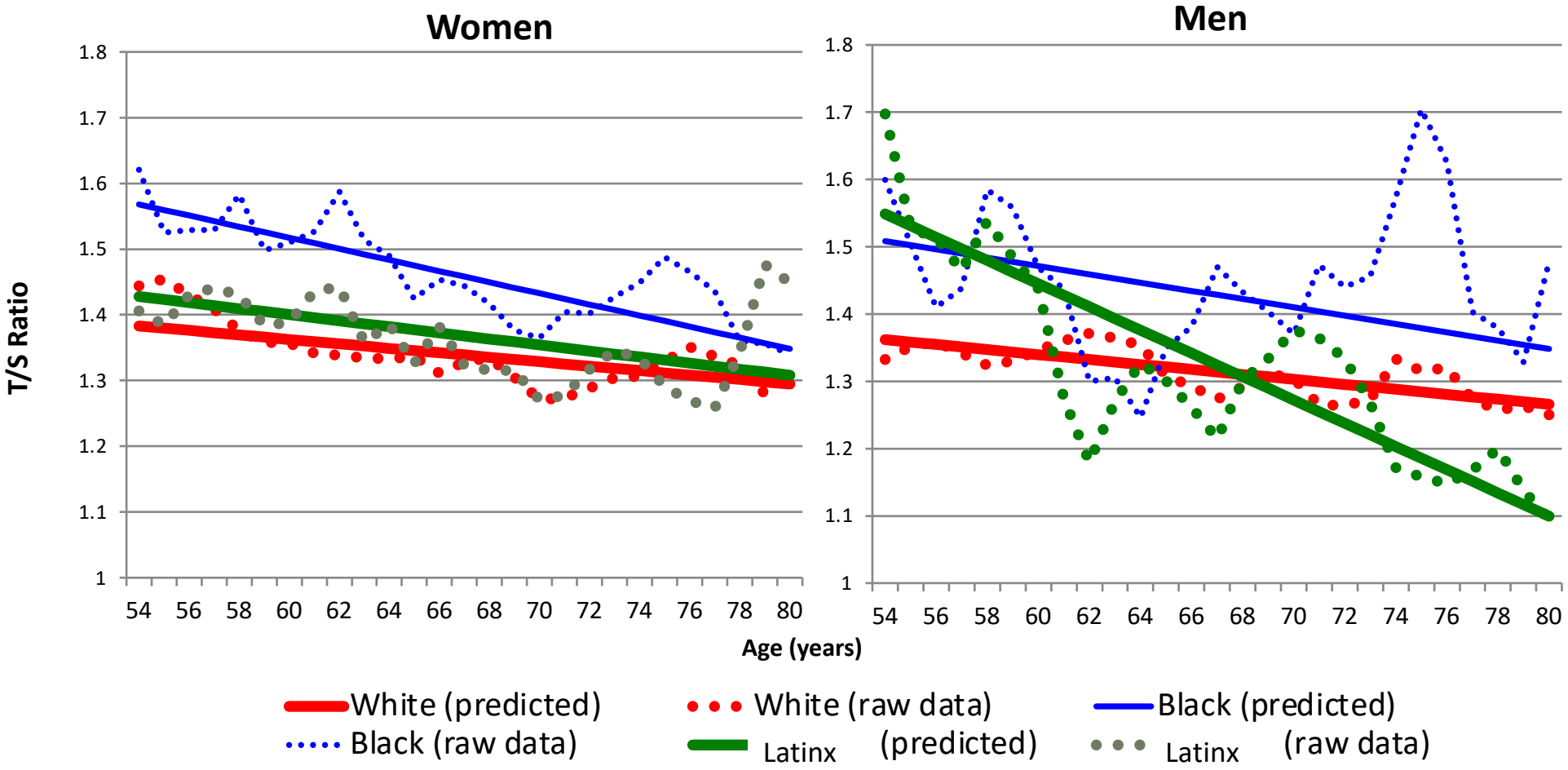
ASSISTANT PROFESSOR

HEALTH MANAGEMENT & POLICY

SDSU SCHOOL OF PUBLIC HEALTH

DECEMBER 4, 2020

Health & Retirement Study: Older Blacks & Latinx adults have longer Salivary TL (STL) than whites (n=5,228) (Brown, Needham & Ailshire, 2017)



Gender stratified models with interactions between race/ethnicity and age adjusting for SES, marital status, employment status, health, and health behaviors.

Gender differences in TL

- Women have long TL than men (see Gardner et al, 2014 for a review)

(NEEDHAM et AL, 2014)

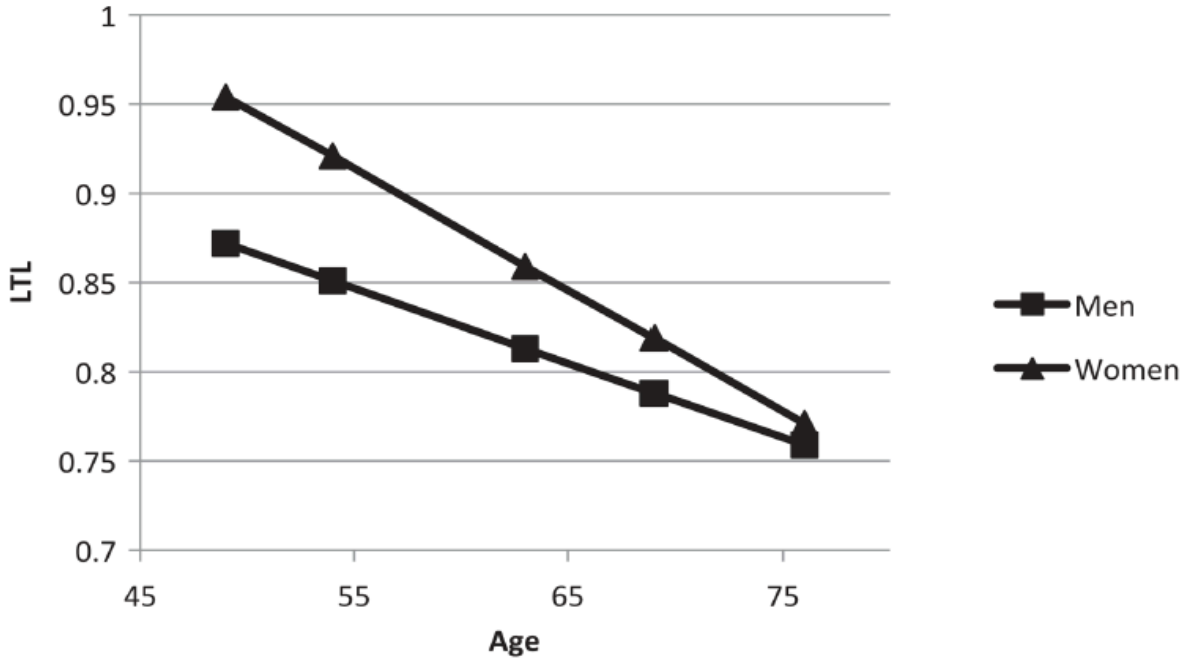


Figure 2.
LTL (T/S ratio) by gender and age (n = 851).

Mixed Findings: TL and race/ethnicity

- Longer TL in Black Americans compared to whites (Adler et al., 2013; Hunt et al., 2008; Needham et al., 2013)
- Shorter TL in Black Americans (Diez Roux et al., 2009; Geronimus et al., 2010)
- No difference in TL among Latinxs compared to whites (Geronimus et al., 2015; Needham et al., 2013)
- Shorter TL in Latinxs (Diez Roux et al., 2009)

(HUNT et AL, 2008)

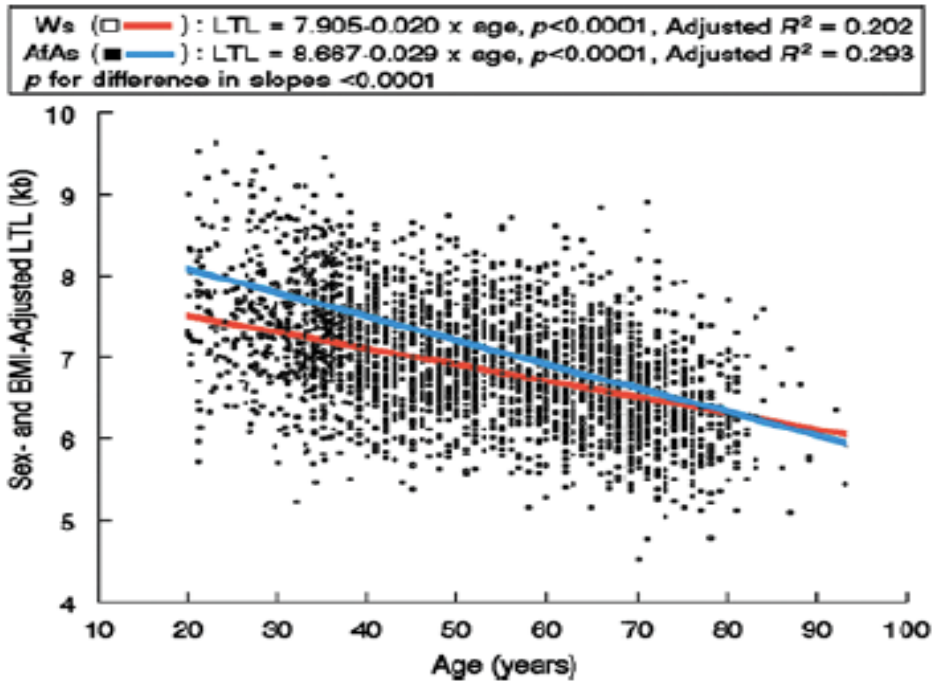


Fig. 3 Sex- and body mass index-adjusted leukocyte telomere length (LTL) vs. age for African Americans and whites from the NHLBI Family Heart Study (FHS) and the Bogalusa Heart Study (BHS) combined.

Research questions

1. Is STL a biomarker of aging that **adds to the explanatory** value of age when predicting high risk performance on indicators of biological, physical, and cognitive function in older adults? (Brown, Zhang, Mitchell, & Ailshire, 2018)
2. Can STL be used to **identify high risk functioning** across a **diverse, nationally representative sample** or help explain **race/ethnic variability** on these same indicators of health across white, black, and Hispanic older adults? (Brown, Garcia & Ailshire, 2020)

Before adjusting for age STL predicts being high risk (n= 5,280)

-HDL Cholesterol
-Total Cholesterol
-Cystatin C
-Pulse Pressure
-BMI (obese)
-Lung function
-Walking speed

Biomarkers	β	SE		β	SE
HDL Cholesterol	0.19	(0.10)	+		
Total Cholesterol	-0.37	(0.13)	**		
HbA1c	0.17	(0.12)			
CRP	-0.07	(0.09)			
Cystatin C	-0.36	(0.18)	*		
Systolic BP	-0.01	(0.09)			
Diastolic BP	0.06	(0.11)			
Heart Rate	-0.09	(0.18)			
Pulse Pressure	-0.23	(0.10)	*		
BMI	0.18	(0.09)	*		
Physical Performance					
Lung Function	0.36	(0.10)	***		
Walking Speed	-0.31	(0.15)	*		
Grip Strength	-0.16	(0.11)			
Balance	-0.09	(0.09)			
Cognition	-0.08	(0.12)			

Logistic regression models adjusting for gender and telomere assay plate

*p<0.05 **p<0.01 ***p<0.001

(Brown, Zhang, Mitchell, & Ailshire, 2018)

Before adjusting for age STL predicts being high risk (n= 5,280)

-HDL Cholesterol
-Total Cholesterol
-Cystatin C
-Pulse Pressure
-BMI (obese)
-Lung function
-Walking speed

After adjusting for age STL only predicts:

-HDL Cholesterol
-Total cholesterol
-Lung function

Logistic regression models adjusting for gender and telomere assay plate

*p<0.05 **p<0.01 ***p<0.001

Biomarkers	β	SE		+Age β	+Age SE	
HDL Cholesterol	0.19	(0.10)	+	0.19	(0.10)	*
Total Cholesterol	-0.37	(0.13)	**	-0.45	(0.14)	**
HbA1c	0.17	(0.12)		0.17	(0.12)	
CRP	-0.07	(0.09)		0.04	(0.09)	
Cystatin C	-0.36	(0.18)	*	-0.12	(0.16)	
Systolic BP	-0.01	(0.09)		0.08	(0.09)	
Diastolic BP	0.06	(0.11)		0.02	(0.11)	
Heart Rate	-0.09	(0.18)		-0.18	(0.19)	
Pulse Pressure	-0.23	(0.10)	*	-0.05	(0.09)	
BMI	0.18	(0.09)	*	0.09	(0.09)	
Physical Performance						
Lung Function	0.36	(0.10)	***	0.23	(0.11)	*
Walking Speed	-0.31	(0.15)	*	0.02	(0.14)	
Grip Strength	-0.16	(0.11)		0.09	(0.11)	
Balance	-0.09	(0.09)		0.10	(0.10)	
Cognition	-0.08	(0.12)		0.10	(0.11)	

(Brown, Zhang, Mitchell, & Ailshire, 2018)

Age predicts biological, physical, and cognitive health before adjusting for STL (n= 5,280)

Biomarkers	β	SE		β	SE
HDL Cholesterol	0.00	(0.00)			
Total Cholesterol	-0.02	(0.00)	***		
HbA1c	0.00	(0.01)			
CRP	-0.01	(0.00)	***		
Cystatin C	0.09	(0.01)	***		
Systolic BP	0.04	(0.00)	***		
Diastolic BP	-0.02	(0.00)	**		
Heart Rate	-0.04	(0.01)	***		
Pulse Pressure	0.07	(0.00)	***		
BMI	-0.05	(0.00)	***		
Physical Performance					
Lung Function	-0.09	(0.01)	***		
Walking Speed	0.15	(0.01)	***		
Grip Strength	0.10	(0.11)	***		
Balance	0.08	(0.09)	***		
Cognition	0.07	(0.12)	***		

Logistic regression models adjusting for gender & telomere assay plate

*p<0.05 **p<0.01 ***p<0.001

(Brown, Zhang, Mitchell, & Ailshire, 2018)

Age predicts biological, physical, and cognitive health before adjusting for STL (n= 5,280)

STL does not explain or add to the predictive power of age.

Logistic regression models adjusting for gender & telomere assay plate

*p<0.05 **p<0.01 ***p<0.001

Biomarkers	β	SE		+ TL β	+ TL SE	
HDL Cholesterol	0.00	(0.00)		0.00	(0.00)	
Total Cholesterol	-0.02	(0.00)	***	-0.03	(0.00)	***
HbA1c	0.00	(0.01)		0.00	(0.01)	
CRP	-0.01	(0.00)	***	-0.01	(0.00)	***
Cystatin C	0.09	(0.01)	***	0.09	(0.01)	***
Systolic BP	0.04	(0.00)	***	0.04	(0.00)	***
Diastolic BP	-0.02	(0.00)	**	-0.02	(0.00)	**
Heart Rate	-0.04	(0.01)	***	-0.04	(0.01)	***
Pulse Pressure	0.07	(0.00)	***	0.07	(0.00)	***
BMI	-0.05	(0.00)	***	-0.05	(0.00)	***
Physical Performance						
Lung Function	-0.09	(0.01)	***	-0.09	(0.01)	***
Walking Speed	0.15	(0.01)	***	0.15	(0.01)	***
Grip Strength	0.10	(0.11)	***	0.11	(0.00)	***
Balance	0.08	(0.09)	***	0.08	(0.00)	***
Cognition	0.07	(0.12)	***	0.07	(0.01)	***

(Brown, Zhang, Mitchell, & Ailshire, 2018)

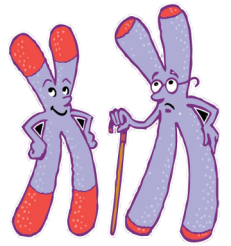
Mixed Findings: TL and indicators of health and aging

STUDIES SHOWING A RELATIONSHIP

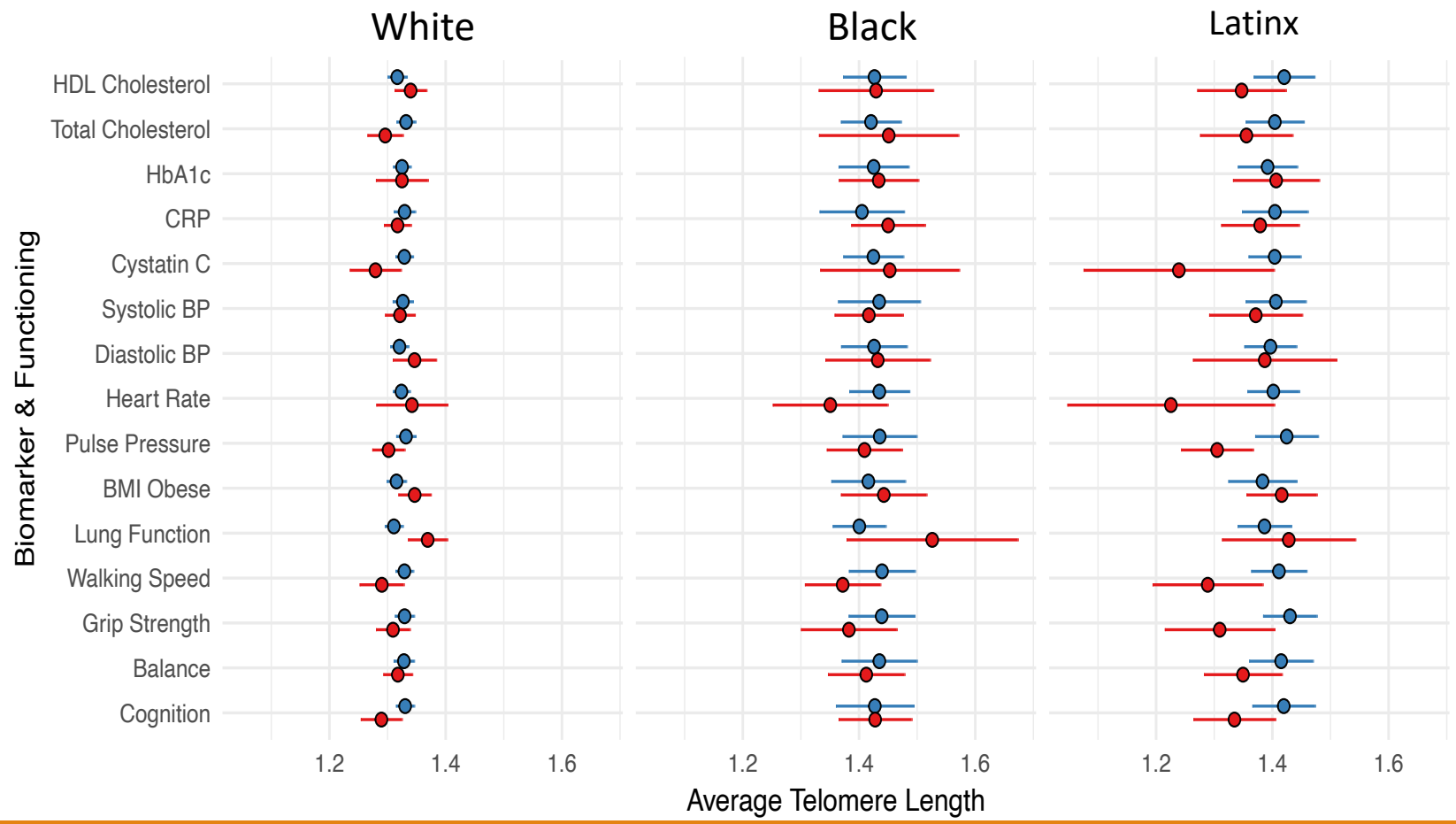
- **Inflammatory markers:** C-reactive protein (CRP), Interleukin 6 (IL-6) (Barbieri et al., 2009; : Kaplan et al., 2009)
- **Cardiovascular markers:** pulse pressure, blood pressure(Aviv, 2001; Anstey, 1996)
- **Functioning:** lung function, handgrip strength(Bekaert et al, 2005; Karasik et al, 2005; Butler et al;. 2004)
- **Cognitive performance**(Valdes et al, 2008; Yaffe al., 2009)

STUDIES SHOWING NO RELATIONSHIP

- (Sanders, 2013)
- (Mather et al, 2010)
- Fitzpatrik, 2007)
- (Mather et al, 2010)
- (Belaert et al, 2005)
- (Harris et al, 2006)
- (Harris et al, 2009)

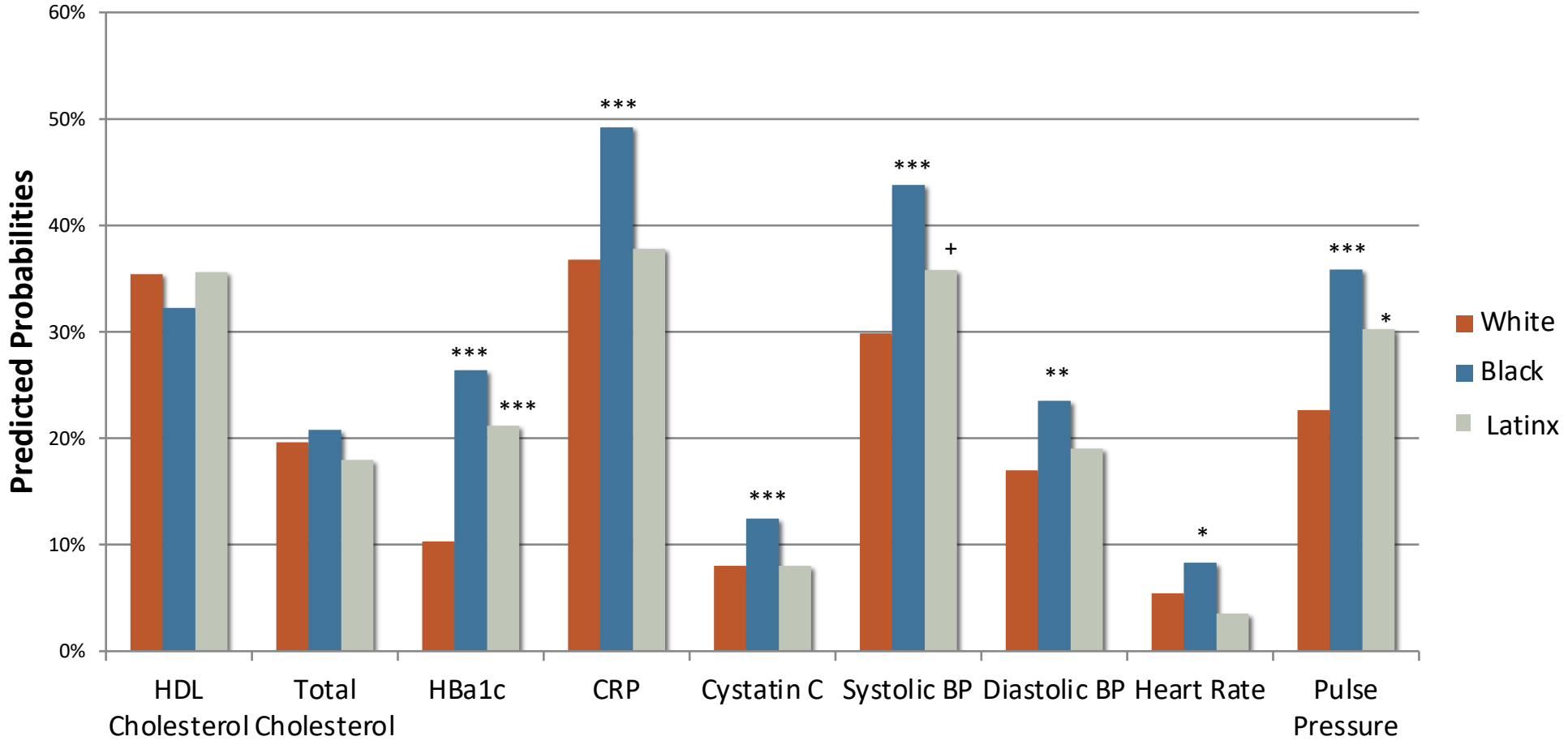


Mean STL by race/ethnicity and high vs. low risk health status (n=4,074)



(Brown, Garcia, & Ailshire, 2020)

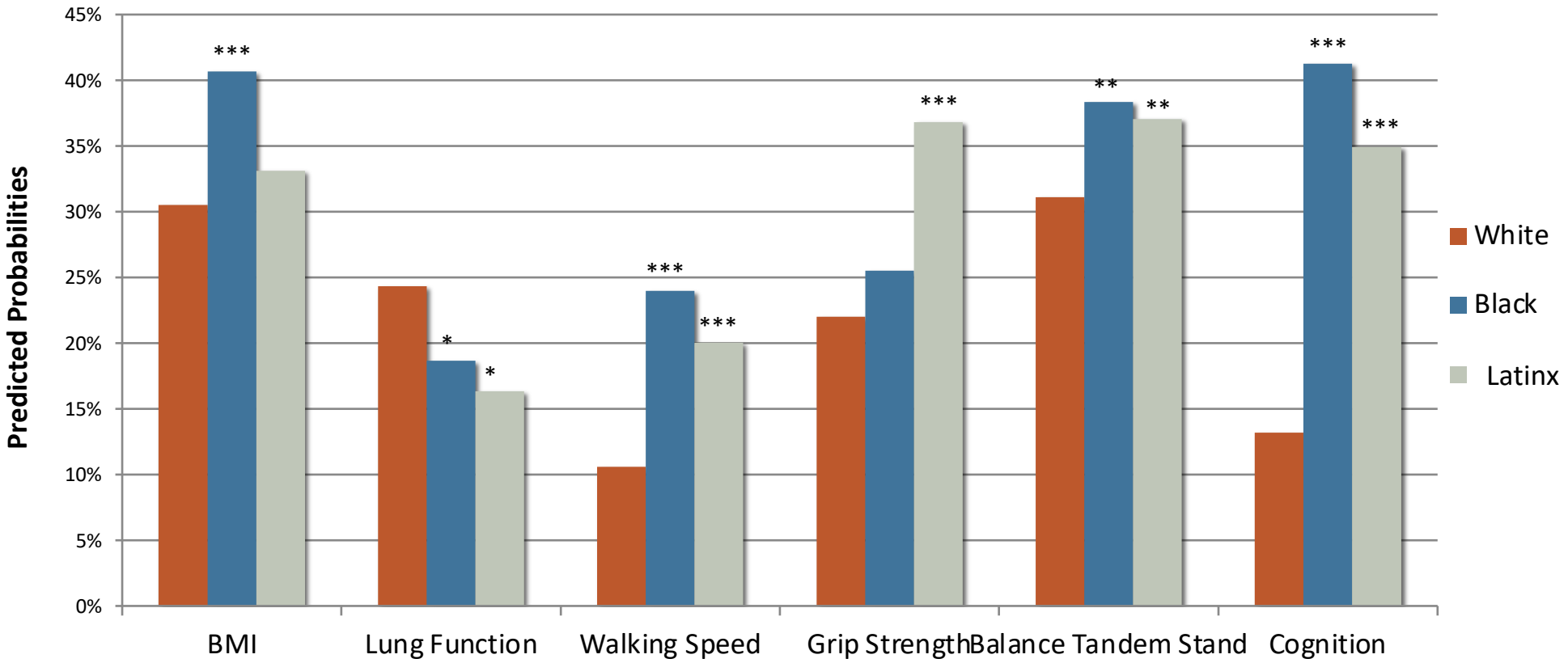
TL does not explain race/ethnic differences in high risk health (n=4,074)



(Brown, Garcia, & Ailshire, 2020)

Logistic regression models adjusting for age, gender TL and assay plate
*p<0.05 **p<0.01 ***p<0.001

TL does not explain race/ethnic differences in high risk health (n=4,074)



(Brown, Garcia, & Ailshire, 2020)

Logistic regression models adjusting for age, gender TL and assay plate
*p<0.05 **p<0.01 ***p<0.001

KHB method (Karlson, Holm & Breen, 2011)

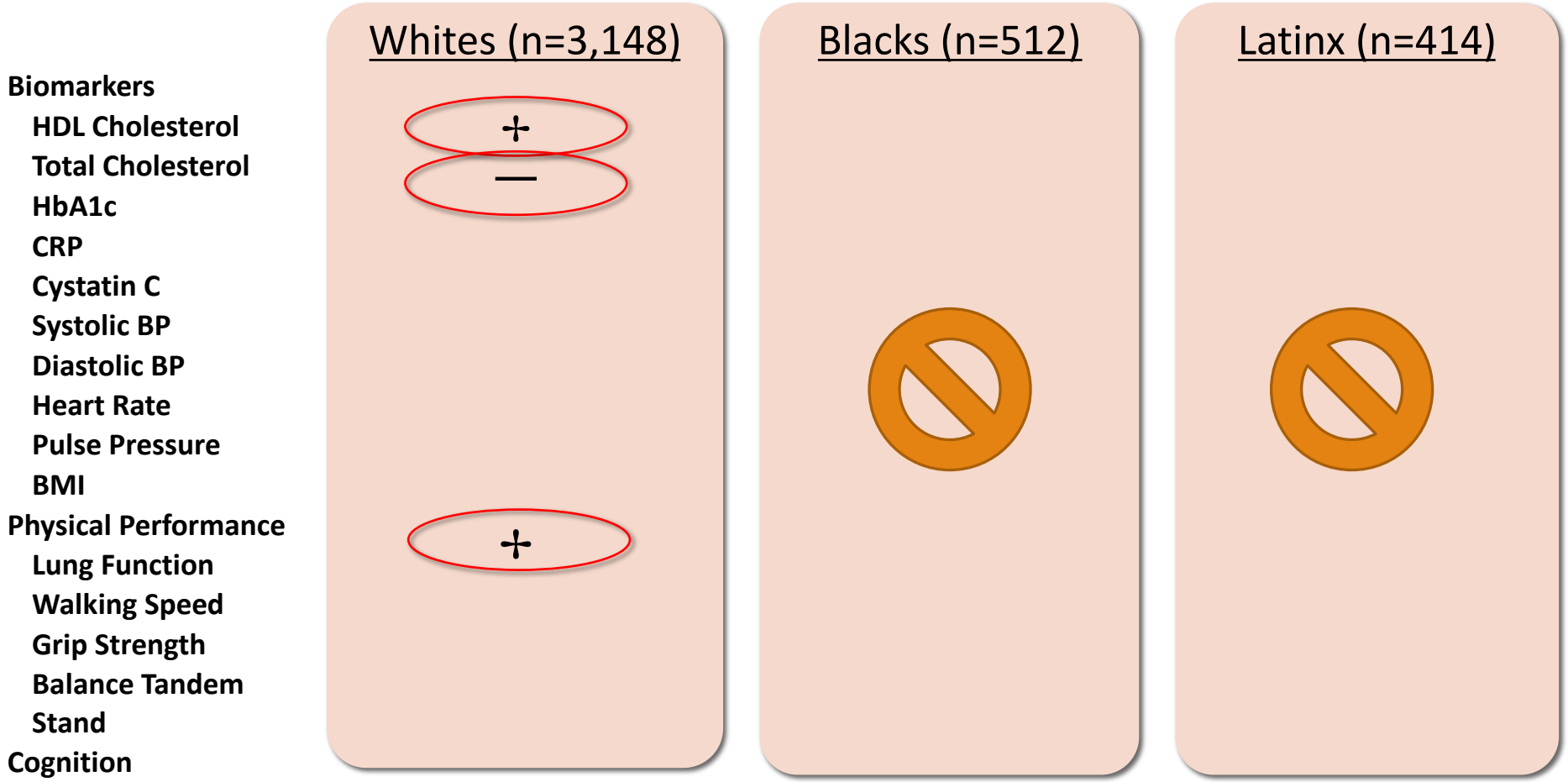
Race/ethnic differences in high risk health are not attributable to the variability in STL across race/ethnic group (n=4,074)

	% Indirect	
	Blacks	Latinx
Biomarkers		
HDL Cholesterol	8.67	30.68
Total Cholesterol	33.37	17.49
HbA1c	0.58	0.38
CRP	1.34	1.58
Cystatin C	1.72	5.65
Systolic BP	0.89	0.80
Diastolic BP	2.48	1.45
Heart Rate	2.69	1.27
Pulse Pressure	0.84	0.60
BMI	2.80	2.62
Physical Performance		
Lung Function	6.71	6.71
Walking Speed	0.28	0.16
Grip Strength	1.16	0.13
Balance Tandem	2.12	0.69
Stand	0.32	0.15
Cognition		

(Brown, Garcia, & Ailshire, 2020)

KHB: % indirect from logistic regression models; adjusts for age, gender, and telomere assay plate.

Stratified models: STL predicts indicators of health only among whites



(Brown, Garcia, & Ailshire, 2020)

Race/ethnic stratified logistic regression models; adjusts for age, gender, and telomere assay plate; Hispanic group adjusted for foreign born status $p<0.05$

TL did not predict nor account for race/ethnic variation in health and functioning

- Race/ethnic stratified models suggest that TL may better characterize health and functioning among older whites
- Race/ethnic variation in STL did not explain race/ethnic variation in health and functioning
- STL in the HRS– measured cross-sectionally in salvia and quantified by qPCR– is not a biomarker of aging that helps us understand race/ethnic differences in older adulthood.
- It maybe worth questioning the value of including STL in large nationally representative studies of older adults.

How do we explain mixed findings in TL?

Methodical issues

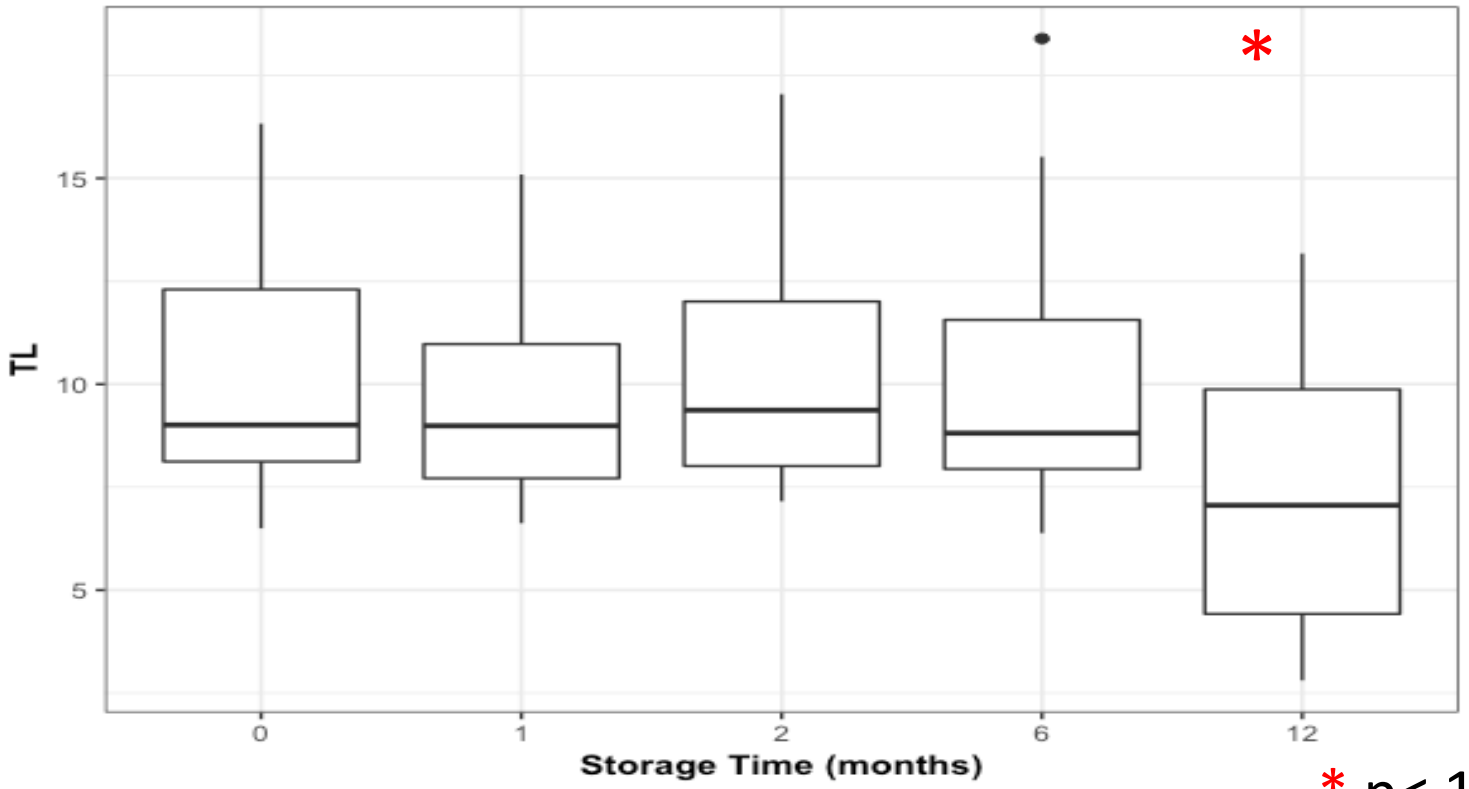
- Cross-sectional data
  - Change more important than absolute TL ?
- Cell type (salvia vs blood)
- Assay (qPCR, southern blot)
- Sample size
- Homogenous samples (race/ethnicity, age, geography)

Highly heritable trait (estimates range from 0.36 to 0.82) (Andrew et al. 2006; Honig et al. 2015)

- Black Americans are born with longer TL (Drury et al., 2015; Rewak et al., 2014)

HRS: Measured STL by storage month (at room temp before extraction) (Faul et al, unpublished)

10.03 (2.65) 9.57 (2.33) 10.03 (2.63) 9.82 (2.80) 7.21 (3.11)



* $p < 10^{*-3}$

HRS 2008 TL data & social factors:

Studies have found links with

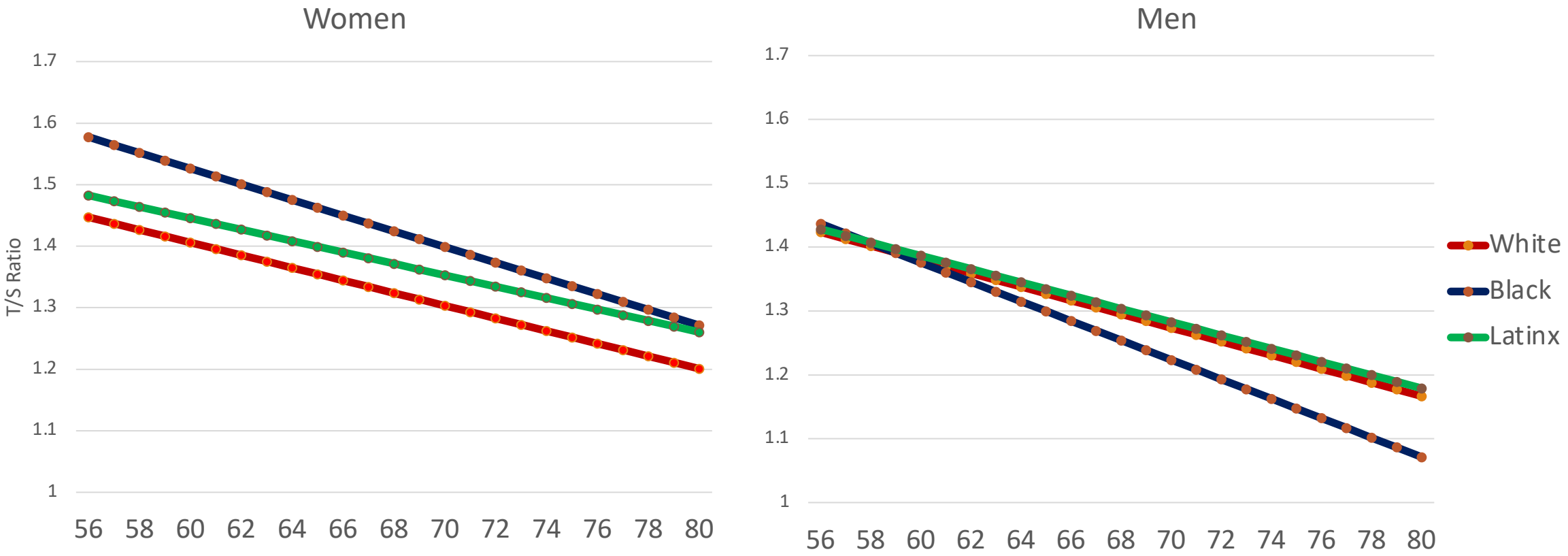
- Social relationships (Lincoln, Lloyd & Nguyen, 2017)
- Religious involvement (Hill et al, 2017)
- Discrimination (Liu & Kawachi, 2017; Lee, Kim & Neblett, 2017)
- Depressive symptoms (Whisman & Richardson, 2017)
- Lifespan adversity (Puterman et al, 2016; Willis et al, 2019)
- Marital disruption (Whisman et al, 2016)

HRS | HEALTH AND RETIREMENT STUDY

2016 HRS Venous Blood Study

- Re-assayed TL from new subsample using venous blood
  - 10mL EDTA (whole blood)
  - Storage: 3.5 mL plasma Buffy coat Extracted DNA
- Real time PCR
- T/S Ratio
  - the ratio of copies of telomere specific sequence to a nuclear gene (albumin) copy number will be determined for each sample and standardized to a reference DNA sample to adjust for assay variability.
- CV= 8%.

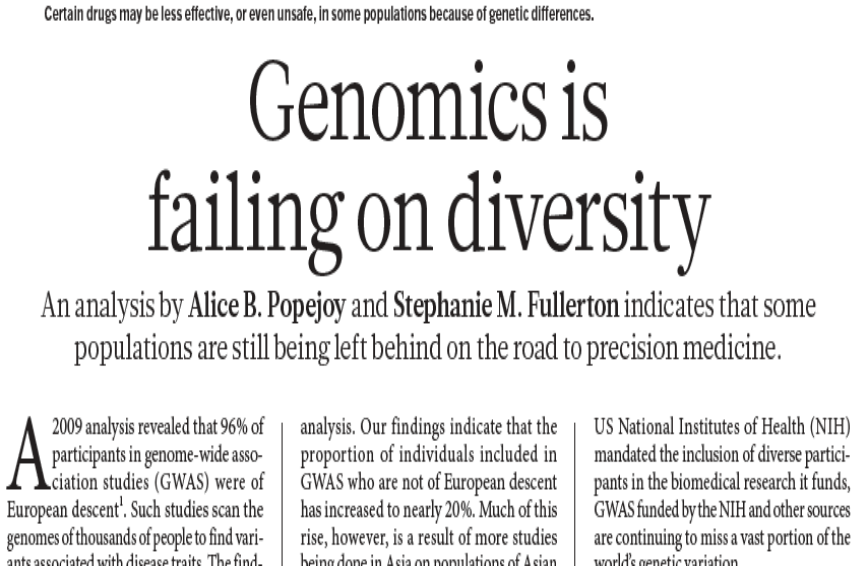
2016 VBS: Older Black women have longer TL (n=3,853)



Gender stratified models with interactions between race/ethnicity and age

Inequalities in health exacerbated by molecular based biomarkers?

- 79 % of all GWAS participants are European Ancestry (Martin et al, 2018)
  - despite making up 16% of global population
- Polygenic risk scores perform better in European populations (Martin et al, 2018)
- African and Asian ancestry
  - more likely to receive ambiguous genetic test results
  - More likely to have variants of unknown significance (Petrovski & Goldstein, 2016)
- African ancestry
  - more likely to be wrongly told that a mutation increases their risk of developing disease (Manrai et al, 2016)



Certain drugs may be less effective, or even unsafe, in some populations because of genetic differences.

Genomics is failing on diversity

An analysis by **Alice B. Popejoy** and **Stephanie M. Fullerton** indicates that some populations are still being left behind on the road to precision medicine.

A 2009 analysis revealed that 96% of participants in genome-wide association studies (GWAS) were of European descent[1]. Such studies scan the genomes of thousands of people to find variants associated with disease traits. The find-

analysis. Our findings indicate that the proportion of individuals included in GWAS who are not of European descent has increased to nearly 20%. Much of this rise, however, is a result of more studies being done in Asia on populations of Asian

US National Institutes of Health (NIH) mandated the inclusion of diverse participants in the biomedical research it funds, GWAS funded by the NIH and other sources are continuing to miss a vast portion of the world's genetic variation

Acknowledgements:

Catherine Perez (University of Nebraska Lincoln)

Yuan Zhang (University of North Carolina)

Jennifer Ailshire (University of Southern California)

Belinda Needham (University of Michigan)

Colter Mitchell (University of Michigan)

Jessica Faul (University of Michigan)

Eileen Crimmins (University of Southern California)

Funding:

National Institute on Aging (T32AG000037 & T32AG000221)

TRN Pilot Grant

THANK YOU!

Email:

Lbrown2@sdsu.edu

Twitter:

@ProfBrownnnn